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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,734	12/15/2005	Timo Heinrich	MERCK-3099	3735

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EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1624	

NOTIFICATION DATE	DELIVERY MODE
12/28/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@mwzb.com

Office Action Summary	Application No.	Applicant(s)	
	10/560,734	HEINRICH ET AL.	
	Examiner	Art Unit	
	NOBLE JARRELL	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,7,9,12 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,2,4,6,7 and 9* is/are allowed.

6)☒ Claim(s) *3,12 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Current Status of 10/560734

1. Prosecution is being re-opened in this case. Claims 1-4, 6-9, 12, and 15 are being examined in the instant application.

Claim Objections

2. Claim 3 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 3 recites two compounds which are not embraced by formula I of claim 1. In claim 1, an indoline ring of formula I is substituted twice on the phenyl portion of the fused ring. Both compounds listed in this claim are substituted once on the phenyl portion of the indoline ring. Consequently, these compounds are not further limiting of claim 1.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 12 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the achievement of anxiolytic, antidepressant, neuroleptic, and/or antihypertonic effect as well as the treatment of migraines and obsessive compulsive disorder, does not reasonably provide enablement for treatment of cerebral infarctions, stroke, or cerebral ischaemia. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention

must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to methods of treating various diseases with compounds of the following structure: a trisubstituted indoline ring connected to a piperidine or piperazine ring by a C_mH_{2m} linker, where m is two to six; the piperidine or piperazine is connected to a benzofuran ring by a C_nH_{2n} linker, where n is zero to four. Thus, the claims taken together with the specification imply that inhibition of 5-HT_{1A} or SSRI can lead to treatment of the disorders recited in claims 12 and 15.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Hoelzemann et al. (DE 10353657, published 23 June 2005) teaches that 5-HT_{1A} antagonism is linked to an anxiolytic, antidepressant, neurloleptic, and/or an antihypertonic effect (abstract).

Schurks (*Expert Opinion on Drug Metabolism Toxicology*, **2009**, *5(9)*, 1141-48) teaches that 5-HT_{1A} is may be responsible for the prophylactic properties of DHE, which itreats migraine headaches (page 1143, section 2.4, "Pharmacodynamics").

Grigoriadis (*Expert Opinion in Therapeutic Targets*, **2009**, *9(4)*, pages 651-684) teaches 5-HT uptake inhibition is linked to anxiety disorder, obsessive-compulsive disorder, and major depressive disorder (table 1, page 654).

Czlonkowska et al. (*Expert Opinion in Pharmacotherapy*, **2009**, *10(8)*, pages 1249-59) teach that cerebral ischaemia has been shown to be part and not part of treatment strategy for stroke (page 1250, column 1, paragraph 3). Table 1 (page 1251, "Serotonerigic Agents" heading) shows that different serotonergic agents yield different results for the treatment of stroke in clinical trials. Whereas fluoxetine worked for the improvement of stroke recovery, moclobemide did not improve stroke recovery. Because cerebral ischaemia is part of treatment strategy for stroke, it is unpredictable whether serontonergic agents can treat cerebral ischaemia as well. Czlonkowska also states that cerebral infarcts are linked to G-CSF (page 1254, section 6.3, "Growth Factors", first paragraph).

(5) The relative skill of those in the art:

Those of relative skill in the art are those with level of skill of the authors of the references cited to support the examiner's position (The relative skill of those in this art is MD's, PhD's, or those with advanced degrees and the requisite experience in treatment of diseases related to 5-HT_{1A} or SSRI reuptake inhibition).

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for the achievement of anxiolytic, antidepressant, neuroleptic, and/or antihypertonic effect as well as the treatment of migraines and obsessive compulsive disorder.

However, the specification does not provide guidance for treatment of cerebral infarctions, stroke, or cerebral ischaemia.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claims 12 and 15 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 3 recites two compounds in which an indoline ring is substituted with a cyano group at its 5-position There is insufficient antecedent basis for this limitation in the claim because claim 1 specifies an indoline ring of formula I is required to be substituted twice on the phenyl portion of the ring. In both compounds of claim 3, the phenyl ring is substituted once. Therefore, claim 3 lacks antecedent basis.

Allowable Subject Matter

7. Claims 1-2, 4, 6, 7, and 9 appear free of the prior art of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NOBLE JARRELL whose telephone number is (571)272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Noble Jarrell/
Examiner, Art Unit 1624

/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624